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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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THOMPSON HINE L.L.P. Intellectual Property Group P.O. BOX 8801 DAYTON, OH 45401-8801			EXAMINER JONES, DAMERON LEVEST	
			ART UNIT 1618	PAPER NUMBER
			MAIL DATE 09/23/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/800,531	Applicant(s) ACHILEFU ET AL.	
	Examiner D L. Jones	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 September 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-35 and 45-52 is/are pending in the application.
- 4a) Of the above claim(s) 45-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 9/9/09 wherein claims 1-31 and 36-44 were canceled; claim 32 was amended; and claim 52 was added. In addition, the Examiner acknowledges receipt of the request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/9/09 has been entered.

Note: Claims 32-35, and 45-52 are pending.

RESPONSE TO APPLICANT'S AMENDMENT/ARGUMENTS

2. The Applicant's arguments and/or amendment filed 9/9/09 to the rejection of claims 32-35 made by the Examiner under 35 USC 103 and/or 112 have been fully considered and deemed persuasive-in-part for the reasons set forth below.

112 First Paragraph Rejection (Scope of Enablement)

The 112, first paragraph, rejection is MOOT in view of the scope of enablement rejection below.

Note: The documents and arguments submitted by Applicant regarding referencing Wikipedia have been reviewed.

112 Second Paragraph Rejection

The 112, second paragraph, rejection is MOOT in view of the 112 second paragraph rejection below.

Note: The documents and arguments submitted by Applicant regarding referencing Wikipedia have been reviewed.

103 Rejection

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 32-35 under 35 USC 103(a) as being unpatentable over Licha et al (US Patent No. 6,083,485) is MAINTAINED for reasons of record in the office action mailed 6/10/09 and those set forth below.

In summary, Applicant asserts Licha teaches away from the use of cyanine dyes as already solving the problem of insufficient fluorescence. Applicant asserts that another teaching away in Licha is that the document teaches that fluorescence may not be desirable. In addition, Applicant asserts that Licha discloses that the purpose for adding cyclodextrin is to enhance stability and solubility of the composition. Thus, it is Applicant's position that it is not obvious to use cyclodextrin to enhance fluorescence as in the instant invention. Also, Applicant asserts that Licha teaches away from Applicant's invention because (1) Licha teaches the use of cyanine dyes as already solving the problem of insufficient fluorescence and (2) Licha teaches that fluorescence may not be desirable.

Applicant's arguments are non-persuasive for the reasons set forth below. First, according to the abstract of Licha et al, it is disclosed that the dyes and their biomolecule adducts may be use as contrast media for fluorescence and transillumination diagnostics in the near infrared radiation range. Thus, a skilled artisan

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would be motivated to use the compounds/compositions of Licha et al for fluorescence purposes. Secondly, a skilled artisan would recognize that a composition is inseparable from its properties. As a result, the properties associated with Applicant combining a cyanine dye and cyclodextrin would be the same as that obtain from Licha et al combining their cyanine and cyclodextrin. Thus, while Licha et al disclose that the addition of cyclodextrin is added for a reason different than that of Applicant, the skilled artisan would recognize that the prior art and the instant invention disclose overlapping subject matter since the same components are added to the compositions.

Furthermore, in response to Applicant's argument that the use of cyclodextrin, in the instant invention, is to enhance fluorescence, the fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Hence, the rejection is deemed proper.

WITHDRAWN CLAIMS

3. Claims 45-52 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

NEW GROUNDS OF REJECTIONS

Double Patenting Rejection

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

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and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 32-35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6-9, 11, 14-16, 24, and 26-29 of U.S. Patent No. 6,423,547. Although the conflicting claims are not identical, they are

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not patentably distinct from each other because both sets of claims are directed to fluorescent relating methods wherein a cyanine dye is used in combination with a compound such as cyclodextrin. The claims differ in that those of the patented invention do not specifically state that the cyclodextrin is added to enhance the florescence. However, it would have been obvious to one of ordinary skill in the art that fluorescence is enhanced because a skilled practitioner would recognize that .a composition is inseparable from its properties. Thus, the properties associated with Applicant's product would also be associated with the claims of the instant invention. Hence, both references disclose overlapping subject matter.

112 First Paragraph Rejection (Scope of Enablement)

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 32-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is reminded that an Inventor is entitled to a patent to protect his work only if he/she produces or has possession of something truly new and novel. The invention being claimed must be sufficiently concrete so that it can be described for the world to appreciate the specific nature of the work that sets it apart from what was

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before. The Inventor must be able to describe the item to be patented with such clarity that the Reader is assured that the Inventor actually has possession and knowledge of the unique composition that makes it worthy of patent protection. The instant application does not sufficiently describe the invention as it relates to the types of cyanine and indocyanine dyes that are compatible with the instant invention. In particular, according to Hawley's Condensed Chemical Dictionary, 2002, 14th Edition by John Wiley & Sons, Inc. (see attachment), a cyanine dye is defined as one of a series of dyes consisting of two heterocyclic groups connected by a chain of conjugated double bonds containing an odd number of carbons. Possible cyanine dyes include isocyanines, merocyanines, cryptocyanines, and dicyanines. In addition, according to Licha et al (US Patent No. 6,083,485), the classes of cyanine dyes are structurally different. For example, in column 5, line 1, Licha et al disclose a general formula for a cyanine dye. In columns 6-7, bridging paragraph, Licha disclose a general formula for merocyanine dyes. It should be noted that the structure of the merocyanine dyes are different from those having the general cyanine dye formula. Other structurally different cyanine dyes include those found in columns 10-11, bridging paragraph (Licha et al) that differ in how the variable Q is defined. Hence, what the Reader gathers from the instant application is a desire/plan/first step for obtaining a desired result. While the Reader can certainly appreciate the desire for achieving a certain end result, establishing goals does not necessarily mean that an invention has been adequately described.

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While compliance with the written description requirements must be determined on a case-by-case basis, the real issue here is simply whether an adequate description is necessary to practice an invention described only in terms of its function and/or based on a disclosure wherein a description of the components necessary in order for the invention to function are lacking. In order to satisfy the written description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the Inventor possessed the claimed invention at the time of filing. In other words, the specification should describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that the Inventor created what is the claimed. Thus, the written description requirement is lacking in the instant invention since the various terms as set forth above are not described in a manner to clearly allow persons of ordinary skill in the art to recognize that Applicant invented what is being claimed.

112 Second Paragraph Rejections

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims as written are ambiguous because it is unclear what cyanine and inodocyanine dyes Applicant is claiming that are compatible with the instant invention.

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103 Rejections

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 32-35 are rejected under 35 U.S.C. 103(a) as being obvious over Rajagopalan et al (US Patent No. 6,423,547).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Rajagopalan et al disclose a composition comprising a carrier-hapten bioconjugate. In particular, the bioconjugate is from a fluorescent dye hapten such as cyanine or indocyanine and the carrier may be cyclodextrin. The bioconjugates are useful in diagnostic and therapeutic medical procedures (see entire document, especially, abstract; column 2, lines 55-58; column 3, lines 4-20). Figure 4 discloses the clearance rate of a composition comprising a cyclodextrin-indocyanine green dye conjugate (column 3, lines 42-43; Figure 4). Likewise, Example 4 (column 7) and Example 12 (column 10) disclose indocyanine/cyanine blue dyes in combination with

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cyclodextrin. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Rajagopalan et al and generate a composition comprising a cyanine dye and cyclodextrin because the prior art discloses that the bioconjugates are formed from fluorescent dyes (i.e., cyanine and indocyanine) in combination with a carrier such as cyclodextrin. Thus, the inventions disclose overlapping subject matter.

In regards to determining the concentration of cyclodextrin necessary to yield 'enhanced' results, the quantity of experimentation needed to be performed by one skilled in the art is reasonable (merely routine). A skilled artisan would be motivated to alter the concentration of the carrier solution to obtain maximum results.

13. Claims 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miwa et al (US Patent No. 7,488,468).

Miwa et al disclose near infrared fluorescent contrast agents and fluorescence imaging (see entire document, especially, abstract). The contrast agent comprises a cyanine dye (column 2, lines 13-40). The near infrared fluorescent contrast agents of Miwa et al disclose a cyanine dye that is suspended or dissolved in a solvent such as injectable distilled water. Additional additives such as cyclodextrin may be added to adjust osmotic pressure and improve stability and solubility (column 65, lines 7-23). Thus, while Miwa et al does not specifically state that their composition is useful in a method of enhancing fluorescence, it would have been obvious to one of ordinary skill in the art at the time the invention was made to generate a composition comprising a

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cyanine or indocyanine dye in combination with a cyclodextrin solution useful in a method of enhancing fluorescence for the reasons set forth below. First, both Applicant and the prior art disclose a cyanine dye that may be used in combination with cyclodextrin. Secondly, both the instant invention and that of the prior art are directed to contrast agents that are useful in a method of fluorescence imaging. Third, while the prior art does not specifically state that the purpose of using cyclodextrin (to enhance fluorescence) is the same as Applicant, the fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). In regards to determining the concentration of cyclodextrin necessary to yield 'enhanced' results, the quantity of experimentation needed to be performed by one skilled in the art is reasonable (merely routine). A skilled artisan would be motivated to alter the concentration of the carrier solution to obtain maximum results. Thus, both Applicant and the prior art disclose overlapping subject matter.

COMMENTS/NOTES

14. It should be noted that the full scope of the instant invention has not been searched.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D L. Jones whose telephone number is (571)272-0617.

The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D L. Jones/
Primary Examiner
Art Unit 1618

September 17, 2009